29 February 2000

DOD RESPONSE TO THE STAFF REPORT OF THE HOUSE GOVERNMENT REFORM'S SUBCOMMITTEE ON NATIONAL SECURITY, VETERANS AFFAIRS, AND INTERNATIONAL RELATIONS ENTITLED, "THE DEPARTMENT OF DEFENSE ANTHRAX VACCINE IMMUNIZATION PROGRAM: UNPROVEN FORCE PROTECTION."

REPORT SUPPOSITION	DOD POSITION	RATIONALE
Because the anthrax vaccine is still being studied as a potential causative or contributing factor in Gulf War veterans' illnesses… (Pg. 1, par. 1)	There is no established connection between the anthrax vaccine and the Gulf War illness. A connection between the two is unlikely.	Several independent national-renowned scientific groups have found no evidence of a link between the anthrax vaccine and Gulf War veterans' illnesses. The Institute of Medicine (1995) concluded that there is no evidence that vaccines caused the non-specific complaints associated with service during Operation Desert Storm. The Presidential Advisory Committee on Gulf War Veterans' Illnesses (1996) concluded that it is unlikely that the health effects reported by Gulf War veterans resulted from anthrax vaccine used alone or in combination with botulinum toxoid vaccine. NIH and Defense Science Board also concluded that the anthrax vaccine did not explain the reported chronic effects associated with GWI.
Against the so-called "asymmetric" threats to U.S. conventional military superiority posed by a growing range of chemical and biological weapons, the anthrax vaccine program represents a medical Maginot	DoD, DIA and CIA believe that this is a valid and serious threat. Several former and potential adversary nations possess weaponized anthrax in several forms - enough to destroy the world's population several times.	As identified by the Chairman of the Joint Chiefs of Staff, anthrax is a major threat to our troops. Anthrax is the primary biological warfare threat faced by U.S. forces. More than 7 countries, including Iraq, Iran, Syria,

Line, a fixed fortification protecting against attack from only one direction. (Pg. 1, par. 3)		and Russia have or are suspected of developing this biological warfare capability. Anthrax is the biological weapon most likely to be utilized because it is highly lethal, easy to produce in large quantities, and remains viable over long periods of time. It is colorless, tasteless, odorless and very difficult to detect. One deep breath is enough to kill an unprotected person. Our vaccine protects against all known strains and all three forms of the disease. To not use it because it only protects against anthrax - the CIA and DIA identified Bio-Weapon of choice - would be ill advised. Protective gear is used in conjunction with vaccination. Research is ongoing to improve and develop detection equipment.
The AVIP lacks a consistent standard of care.(Pg. 1, par 2)	DoD has very sound Clinical Practice Guidelines and standards of care as well as a sophisticated tracking system. It also has a responsive and effective adverse reaction reporting and follow-up system. This includes an independent civilian review committee.	Clinical Practice Guidelines for administering the vaccine and for managing adverse events after vaccination, are in place and very comprehensive. Our system is designed to tell what person received what shot on what day and from what lot. Unlike other vaccines that afford protection after a single dose, anthrax vaccination requires 6 doses over 18 months. So, we must begin administering the vaccination to the entire force early, in

		order to protect the active and reserve forces for future conflicts.
The AVIP… is designed to reach far beyond those at risk. (pg. 1, par 2)	All of our servicemen and women are potentially at risk.	In at least two major theatres, thousands of troops go to work every day under the threat of weaponized anthrax. Many others fly or sail in and out of these areas. Many more are listed as first responders and as reinforcing units. All of our force is subject to terrorist attack by anthrax. At least two groups have it. One has tried to use it. It is strategically unwise to wait for an attack before implementing the program.
Heavy handed, one-sided informational materials only fuel suspicions the program understates adverse reaction risks in order to magnify the relative, admittedly marginal, benefits of the vaccine (Pg. 2, par. 3)	DoD's informational materials are straightforward and fact based. Adverse reaction risks are stated exactly as we know them and as recorded by FDA and VAERS. The benefits are anything but marginal.	"With respect to risk communications, again a major change is taking place. For this and future such programs, the troops are being clearly advised, up front, why the vaccination is needed, what vaccination they are receiving, the safety and efficacy of the vaccine, and what potential adverse effects could occur. It is important that the troops understand the benefits as well as the risks, though very low, of anthrax immunization. When the program starts in a particular unit, troops are given the opportunity to ask questions of the Commanders and medical personnel." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* The statements in our informational materials are

		medically responsible, scientifically accurate and professionally ethical. Although suspicions have certainly been fueled, we would contend they have been motivated by opponents of AVIP, of vaccines in general, of strong national defense, etc., and not by our informational materials. Education of commanders and medical personnel is accomplished through standardized briefings and other informational materials. These educational materials were a major component of AVIP execution from the beginning of the program in Mar 98.
The decision to use the 1950's era vaccine, which requires an elaborate inoculation regime of six shots over 18 months, presents daunting, perhaps insurmountable, logistical challenges to reach a force of 2.4 million active duty and reserve component members. (Pg. 2, par. 5)	There are many vaccines that were developed in the 1950's and earlier that are currently still in use in the United States. This one was, for the record, actually licensed in 1970 and represents an improvement over the 1950's vaccine. It was re-evaluated in 1980 when biomedicine responsibility was transferred from NIH to FDA. At that time it was re-certified safe and effective. DoD is aware of the logistical challenge with the dosing schedule. Services use automated tracking systems to manage the administration in accordance with the FDA approved dosing schedule. Shipping and distribution of	"The only known effective prevention against anthrax is the anthrax vaccine. Treatment of cutaneous anthrax infection involves administration of antibiotics. In the case of pulmonary anthrax infection, therapy has been of limited benefit, except when given immediately after exposure". *Statement by Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999*

	the anthrax vaccine is a world-class successful operation.	"Prior to use of the anthrax vaccine, cases of human anthrax infection in the United States were much more prevalent. According to data from the Centers for Disease Control and Prevention, (CDC) there were approximately 130 reported cases of anthrax infection per year at the start of this century. In the past decade, there have been years with no reported cases of human anthrax infection in the United States. It is difficult to assess exactly how much of this dramatic reduction is due to the vaccine, but immunization with the anthrax vaccine of people at risk, along with vaccination of animals against anthrax, have likely contributed to this favorable decline. Elsewhere in the world, human anthrax cases continue to be reported, especially in countries with predominately agricultural economies." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* "Based upon their review of available data, the Advisory Review Panel recommended

		that the anthrax vaccine manufactured by Michigan Department of Public Health be classified as a Category I product and that appropriate licenses be continued based upon substantial evidence of safety and effectiveness of this product. The safety data from the CDC trials and the efficacy data from the Brachman et al. trials were the basis for these findings. These findings were published in the *Federal Register* on December 13, 1985." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* The GAO recognized the DoD's "well designed and administered packing and shipping" of anthrax vaccine in its Oct 99 report: "DoD Faces Challenges in Implementing Its Anthrax Vaccine Immunization Program."

The sole-source procurement strategy leaves the program vulnerable to supply shortages and price increases. (Pg., 2, par. 6)	The cost of AVA is one of the lowest for any vaccine. Several foreign countries have offered to pay from 2 to 5 times the DoD contracted price.	Sole-source vaccine production is common in the US. Many vaccines licensed in the US are from sole-source vendors: Japanese encephalitis, Lyme borreliosis, Measles, Mumps, Plague, Poliovirus inactivated, Rubella, Typhoid (oral), Chicken Pox, and Yellow Fever. DoD is aware of possible vaccine shortages and designed a phased implementation to address this challenge. Phased implementation is directed in each Service Implementation Plan. CDC's web site lists the cost of many vaccines. Adult vaccine costs range from $16 to $35 per dose. AVA increased from $4.44 per dose, in the first contract, to $10.64 per dose in the second contract. *CDC Pricetable, 2 August 1999.*

As a result (of sole-source procurement) DoD and the sole vaccine maker are locked in a mutually dependent relationship. (Pg. 2, par. 6)	DoD has entered in a **contractual** basis with BioPort Corporation to produce AVA. Anthrax vaccine is a key element in protecting service members against the lethal threat of anthrax. DoD is working with BioPort, the only licensed anthrax vaccine manufacturer to ensure there is a supply of this safe and effective vaccine. *Statement by Brigadier General Eddie Cain, Joint Program Manager, Joint Program Office for Biological Defense, Falls Church, Virginia, Before the National Security, Veterans Affairs and International Relations Subcommittee on Government Reform, First Session, 106th Congress, Anthrax Vaccine Immunization Program (AVIP) April 29, 1999.* We are also pursuing a second source, but in order to meet FDA requirements at a new facility, this effort will require several months to years to complete.	"The BioPort Corporation facility in Lansing, Michigan is the only manufacturer licensed by FDA to manufacture anthrax vaccine. Originally, the facility was operated by the Michigan Department of Public Health. In 1996, the facility became known as the Michigan Biologics Products Institute (MBPI), an entity controlled by the State Government of Michigan. Currently, the facility is known as BioPort Corporation based upon the September 1998 transfer of ownership from MPBI to BioPort Corporation." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* A second manufacturer would be required to submit a supplemental application and pass detailed FDA approval inspections.

The manufacturer, struggling to reopen a plant with a checkered regulatory history, clings to a captive customer. (Pg. 2, par. 7)	MBPI began, and BioPort Corporation continued and completed renovation of the AVA production suite and is now in the normal process of FDA certification under a Biologics License Application (BLA) Supplement. BioPort Corporation produces four other products sold to domestic and international markets so they are not dependent on a single customer.	In their 26 Nov 99 written response addressed to Congressman Dan Burton, FDA stated, "A review of inspection reports from 1972 to 1998 shows the Anthrax Vaccine Adsorbed was covered as part of the inspection on 12 separate occasions either by record review, observation of manufacturing areas or interview with engineering and manufacturing staff." This FDA letter is never acknowledged in the Subcommittee's Report. "The FDA conducted an inspection of MBPI in November 1996. During that inspection, FDA investigators documented numerous significant deviations from the Federal Food, Drug, and Cosmetic Act, FDA's regulations and the standards in MBPI's license. Based upon the documented deviations, FDA issued a Notice of Intent to Revoke Letter (NOIR) to MBPI in March 1997. The NOIR letter did not mandate the closure of the facility or lead to seizure of finished product. The letter, however, did state that if MBPI's corrective actions proved to be inadequate, they would run the risk of having their license revoked. MBPI responded to the NOIR with a "Strategic Plan for Compliance" presented to FDA in April 1997. This plan

		called for the periodic submission of data to FDA that would serve as evidence of MBPI's progress towards achieving compliance with FDA's regulations. Under the plan, FDA would review this data and then monitor MBPI's progress through follow-up inspections. In February 1998, FDA conducted a follow-up inspection of the MBPI facility to evaluate MBPI's compliance with its strategic plan. The February 1998 inspection disclosed significant deviations from FDA's regulations. These deviations included, but were not limited to, the manufacture of the anthrax vaccine. In addition, the inspection resulted in a request by FDA that MBPI quarantine 11 lots of anthrax vaccine held in storage, pending review of additional information to be submitted by BioPort… These lots are still in quarantine, and will remain in quarantine until the company submits required information to the Agency. FDA noted that MBPI had made progress in achieving its compliance goals, but additional work remains in order to correct the deviations related to the manufacture of the anthrax vaccine. Pursuant to its purchase of the MBPI facility in September 1998, BioPort agreed to abide by the strategic plan and other

		commitments for corrective actions made by the management of MBPI. It should be noted that MBPI halted production of anthrax vaccine sublots in January 1998 to begin a comprehensive renovation of the anthrax production facilities." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* BioPort now has a very modern production suite run by knowledgeable professionals. They have satisfactorily resolved the majority of noted discrepancies. The others are in work. Approval for new production is expected by fall of 2000. BioPort Corporation also produces Diphtheria-Tetanus (DT) Pediatrics, Rabies Vaccine Adsorbed, Immune Globulin (Human), as well as Albumin (Human), which target domestic and international markets.
Adverse events following vaccination are reported by women at twice the rate among men. (Pg. 3, par. 1)	This was found to be true in two DoD studies, however, a significant number of the reactions reported were minor	Adverse events (local reactions) following vaccination are reported by women at twice the rate

	local reactions and readily spontaneously resolved.	compared to men. "With regard to safety data, FDA and CDC jointly operate a system called the Vaccine Adverse Event Reporting System (VAERS). FDA uses this system to track adverse events possibly associated with licensed vaccines. Reporting of adverse events associated with the use of anthrax vaccine is voluntary for individual healthcare providers. The vaccine manufacturer, however, must report to FDA all reports of adverse events of which they are aware. The report of an adverse event to VAERS is not documentation that a vaccine caused the event, only that the event occurred after the vaccine was administered. Doctors and other healthcare providers are encouraged to report serious or unexpected adverse events following vaccination, whether or not they believe that the vaccination was the cause of the adverse event. Since it is difficult to distinguish a coincidental event from one truly caused by a vaccine, the VAERS database contains events of both types. It should be emphasized that adverse event reports can be made by a health care professional, a patient or anybody else. If a patient's physician does not file a VAERS report, the patient can do so. FDA encourages individuals to report to VAERS any

		clinically significant adverse event occurring after the administration of any vaccine licensed in the United States. Reports to VAERS may be made in writing or by calling a toll-free number, 1-800-822-7967. Reporting instructions are available on the Internet at www.fda.gov/ cber/vaers.html." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999.* A CDC-supervised study is in progress to determine gender differences and, if appropriate, to recommend, to the FDA, a reduced shot regimen, as female immunity appears to increase faster than male immunity.
Preposterously low adverse report rates generated by DoD point to a program far more concerned with public relations than effective force protection or the practice of medicine. (Pg. 3, par. 1)	We disagree. VAERS reports can be filled out by any medical person giving the shots, any person receiving a shot, or any person treating a suspected reaction. There is no time limit in when they can be submitted and they are not discouraged in any way. DoD updates all educational materials regularly, reflecting the most up-to-date side effect	"From the time the VAERS system started operating in 1990 until April 1, 1999, there have been 101 reports of adverse events associated with use of the anthrax vaccine reported to the VAERS system. Of those, 87 were non-serious events and 14 were considered serious events. Non-serious events included the following symptoms: injection site

	and adverse event data available in order to keep its patients fully informed.	edema (swelling with fluid in tissue), injection site hypersensitivity, rash, headache and fever. Of the 11 serious reactions reported during the current anthrax vaccination program, most individuals have recovered. Three patients were hospitalized for injection site reactions. One individual experienced a more widespread allergic reaction. One individual was hospitalized with a confirmed case of aseptic meningitis nine days after vaccination. Another individual experienced Guillain-Barré syndrome within 24 hours of the third dose. He was unable to walk for nine days. He gradually recovered and his symptoms resolved within five months of the vaccination. Three weeks after receiving the vaccine, another individual experienced a bipolar disorder and thus for has not recovered. It should be emphasized, once again, that it is not always possible to attribute a cause and effect relationship between a reported event and a vaccination. With the exception of injection site reactions, all of the adverse events noted above do occur in the absence of immunization. While the data gathered from the VAERS system can serve

		as a useful tool in spotting potential problems, the data gathered from the VAERS reports on anthrax vaccine, thus far, do not signal concerns about the safety of the vaccine. As more people receive the vaccine, the numbers of adverse events reported will increase." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999.*
Administration of the anthrax vaccine for mass prophylaxis against biological warfare should be considered an off-label use of the product to treat an indication for which it is not explicitly licensed. (Pg. 3, par. 3)	FDA has confirmed repeatedly that AVA use against biological warfare is not an off-label use. DoD requested in writing an opinion on this issue from the FDA prior to the announcement of the program.	Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores. It is also recommended for high-risk persons such as veterinarians and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not

		recommended. If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection. *Anthrax Vaccine Adsorbed Package Insert, BioPort Corporation, Lansing, Michigan U.S. License No. 1260.* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of Anthrax Vaccine protects against inhalation anthrax. Therefore, I believe your interpretation is not inconsistent with the current

		label." From the FDA's 26 Nov 99 letter addressed to Congressman Dan Burton, "Use of the vaccine for protection against both cutaneous and inhalation anthrax exposure is not inconsistent with the labeling for Anthrax Vaccine Absorbed." Further, "There is presently no basis for concluding that the anthrax vaccine, a licensed product, when used in accordance with current labeling, should be used pursuant to an IND application or, as requested in your letter, that FDA 'place the anthrax vaccine back under IND status'." The contents of this letter are never referenced in the Subcommittee's report.
DoD's operational use of a standard of "functional protection" after three inoculations constitutes a *de facto* alteration of the approved six shot regimen. (Pg. 3, par. 3)	DoD's service implementation plans and all subsequently published policies direct and emphasize the adherence to the FDA approved dosing schedule of six doses over 18 months. We do not, have not and do not plan to intentionally deviate from FDA's approved dosing schedule.	At risk individuals who start the series of anthrax vaccinations are required to continue them. After receiving the first three doses, studies indicate that 93-95 % of the individuals will have an immune response. That does not mean that DoD deviates from the protocol. It is only a sign that if one were exposed before completing the protocol, he or she would have a better chance of survival than an unvaccinated person would. For individuals remaining under the program, the FDA protocol is only interrupted due to events such as illness, absence from duty

		or an adverse reaction. This point was made several times during sworn testimony. DoD does not understand how this allegation can continue to show up in subcommittee documents.
The AVIP is a well-intentioned but over-broad response to the anthrax threat. (Pg. 4, par. 1)	AVIP is an appropriate response to the threat.	Force health protection encompasses both preventive and medical intervention as well as personal protective equipment and procedures. We have good protective clothing and equipment, but you cannot fight in it for long periods of time. In addition, our troops might not be wearing the gear when the invisible spore-containing aerosol is dispersed. We may not know an attack has occurred until members become ill or symptomatic. We have some early state of the art detectors, but they lack the sensitivity and quick analytical capability to be effective. Anthrax kills and kills quickly. The enemy has it and it is easy to employ. If you breathe it, and are not vaccinated, you will die. The lethality of inhalation anthrax was impressively demonstrated by the numerous fatalities that occurred after the unintentional release of anthrax spores from the factory in Sverdlovsk, Russia in 1979.

		Vaccination will save the lives of our service men and women if exposed. It is also a huge deterrent to the use of weaponized anthrax and to other bio-weapon development. It would be a dereliction of duty not to provide such protection.
The AVIP is vulnerable to supply shortages and price increases. (Pg. 4, par. 2)	DoD has confidence that the manufacturer will comply with the contract. The cost of AVA is one of the lowest for any vaccine. The DoD constructed the implementation of the program in three phases to accommodate a stockpile of vaccine and knowledge that a new production suite would require FDA certification.	Research and development on a second-generation, recombinant vaccine would take years to accomplish and would not have as much safety history as the current licensed vaccine. A second source of production is being pursued, as well as a second site for testing, certification, storage and shipping.
The AVIP is logistically too complex to succeed... Using an artificial standard that counts only shots more than 30 days overdue, DoD tolerates serious deviations from the Food and Drug Administration (FDA) approved schedule. (Pg. 4, par. 3)	DoD policy is to adhere to the FDA schedule. DoD is aware of the logistical challenge with the dosing schedule and had the Services have designed automated tracking systems to manage the administration in accordance with the FDA approved dosing schedule.	Management tools are used as predictive, current and trailing indicators of performance and timeliness of vaccinations. Protocols are not always precise to the hour and the day, but they are very close. The number of vaccination sites has been increased to ease this challenge, by using VA and civilian hospitals and clinics. Deployable medical teams are also available when required.
Safety of the vaccine is not being monitored adequately. (Pg. 4, par. 4)	Recognizing that this is the largest use of AVA, a safety program was designed by DoD and articulated during the multiple Subcommittee hearings.	The DoD Safety program was described in detail during testimony to the Subcommittee on National Security, Veterans Affairs and International Relations. None of this testimony is reflected

		in the Subcommittee's report. As reported by Major General Claypool, "DoD conducts an aggressive, multi-faceted surveillance program to assess vaccine safety. In fact, the safeguards of vaccine administered to DoD personnel meets or exceeds every standard for vaccine administration to the civilian population. The DoD program uses three scientific methods to evaluate safety, clinical studies, database studies and spontaneous reports (passive surveillance). The extent of this safety surveillance far exceeds any vaccine program in the United States for both childhood and adult vaccines."
…DoD institutional resistance to associating health effects to the vaccine. (pg. 4, par. 4)	There is no institutional resistance to associating health effects with the vaccine.	Every person taken ill either before or after vaccination receives treatment, diagnosis and follow-up. It is unfounded slander against our doctors, nurses, and other medical professionals to make such a statement.
Efficacy of the vaccine against biological warfare is uncertain. (Pg. 4, par. 5)	The FDA and many prominent groups have sited AVA as efficacious against inhalational anthrax bacillus.	"With respect to efficacy, a FDA Advisory Panel stated in 1985 that there is sufficient evidence to conclude that the anthrax vaccine is effective under the limited circumstances for which this vaccine is employed. In a March 13, 1997 memorandum, the FDA confirmed that the pre-exposure administration of the FDA-licensed anthrax vaccine for the prevention of inhalation anthrax is not

		inconsistent with the current product label. In addition, the Committee on Infectious Diseases, American Academy of Pediatrics (1994), states that 'the vaccine is effective in preventing or significantly reducing the occurrence of cutaneous and inhalation anthrax in adults'." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* "Several studies performed at the USAMRIID have demonstrated the efficacy of the FDA-licensed anthrax vaccine against inhalation anthrax in rhesus monkey challenge studies. These animal studies showed that the FDA-approved anthrax vaccine provided greater than 95% protection against high-dose aerosol challenge with anthrax in the monkey model. Human antibody response to the FDA-licensed vaccine provides further suggestive evidence that the FDA-licensed anthrax vaccine will protect against inhalation anthrax." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* The Brachman study (1962) involving four mills in the northeastern United States reported of 5 cases of inhalation anthrax (4 fatal) that occurred in the

		unvaccinated population. The vaccinated population, working in the same mills, had no cases of inhalation anthrax and no deaths. In the Soviet Union, at Sverdlovsk a release of aerosolized anthrax caused at least 68 deaths in an unvaccinated population.
A physician reviewed the AVIP program plans. (Pg. 8, par. 4)	DoD conducted a "detailed, deliberative process" spanning almost four years, prior to approval of this program. It then requested an independent expert to review the health and medical aspects of the program.	Dr. Gerald Burrow, who conducted the independent review, was Dean of Yale University Medical School, special advisor to the President for Health Affairs, David Page Smith Professor of Medicine, a professor of Obstetrics and Gynecology and was a noted participant in other studies and research.
Communication plans were approved centered around a "tri-fold" brochure to be given to service personnel. (Pg. 8, par. 4)	Communication plans are detailed in the service plans and are much more elaborate than distribution of a single "tri-fold".	Communication plans were developed and implemented within each Service. DoD Commanders and Health Care Provider briefings and brochures were developed through working groups representative of all of the Services and DoD. All service plans and training material have been distributed electronically, in written format or via the web site www.anthrax.osd.mil. In addition, lectures have been given, films have been produced and a "1-800" hotline phone number was established to provide 24 hour-a-day question and answer capability (1-877-GET VACC).

On May 18, 1998, Secretary Cohen pronounced the four conditions fulfilled and approved the total force program, which began in September with troops in Korea. (Pg. 8, par. 5)	Supplemental testing is on going. Only anthrax vaccine lots both released by the FDA and supplementally tested are used in the DoD AVIP.	"The Secretary of Defense (SecDef) announced in his December 15, 1997 press release that the Anthrax Vaccine Immunization Program (AVIP) would start only after several conditions were met. One of those conditions was 'supplemental testing to assure sterility, safety, potency and purity of the vaccine'. FDA had previously released these anthrax vaccine lots for use. DoD, however, for added assurance directed JPO-BD to contract with BioPort, formerly Michigan Biologic Products Institute (MBPI), to conduct supplemental testing, with external oversight, on all lots of anthrax vaccine in the DoD stockpile. The supplemental testing is based on tests required by FDA for lot release, and provides an added level of confidence in the potency and purity of the anthrax vaccine in our stockpile. BioPort has performed, and continues to perform supplemental testing on all licensed lots of anthrax vaccine that were in DoD's original stockpile. Mitretek Systems Inc. performs independent oversight and provides a quality assurance function for DoD within the BioPort production facility. Mitretek's staff observes all aspects of the supplemental testing and provides a written report to JPOBD on the acceptability of the testing and test results. JPOBD reviews

		all data prior to releasing any lot for shipment and use. Supplemental testing began in January 1998, and originally was scheduled for completion in November 1998. As of April 1999, eight licensed lots have passed all supplemental testing requirements. JPOBD has approved these eight lots for use." *Statement by Brigadier General Eddie Cain, Joint Program Manager, Joint Program Office for Biological Defense, Falls Church, Virginia, Before the National Security, Veterans Affairs and International Relations Subcommittee on Government Reform, First Session, 106th Congress, Anthrax Vaccine Immunization Program (AVIP) APRIL 29, 1999*
Subsequent FDA review of the studies in 1985 concluded the vaccine was safe, "fairly well tolerated," and effective against cutaneous anthrax, but that data from both human and animal tests was insufficient to support a finding of efficacy with regard to airborne exposure (Pg. 10, par. 3)	Efficacy is based in part on the Brachman study and further substantiated in Rhesus monkey trials.	"Conducting lethal challenge studies in humans is considered unethical and, since there is no study population identified as being at high risk for inhalation anthrax, directly determining the efficacy of the vaccine in humans against aerosol exposure to anthrax spores is not possible. There have been numerous studies of the anthrax vaccine involving animal models. Several studies performed at the USAMRIID have demonstrated the efficacy of the FDA-licensed anthrax vaccine against inhalation anthrax in rhesus monkey challenge studies. These animal studies showed that the

		FDA-approved anthrax vaccine provided greater than 95% protection against high-dose aerosol challenge with anthrax in the monkey model. Human antibody response to the FDA-licensed vaccine provides further suggestive evidence that the FDA-licensed anthrax vaccine will protect against inhalation anthrax." *Prepared statement of Dr. Sue Bailey, Assistant Secretary for Health Affairs, DoD, NSVAIR Anthrax Hearing (I).* The Brachman study indicating that NO cases of inhalation anthrax have occurred in fully vaccinated subjects while the risk of infection continued. These observations lend further support to the effectiveness of this product. "This vaccine is recommended for a *limited, high-risk of exposure population* along with other industrial safety measures designed to minimize contact with potentially contaminated material. The benefit-to-risk assessment is satisfactory *under the prevailing circumstances of use." Federal Register, 21 CFR Part 610, December 13, 1985.* In the nonhuman primate studies, a total of 62 (94%) of the 65 animals vaccinated with AVA survived a highly lethal challenge of aerosolized anthrax. Whereas, of the 18 controls (unvaccinated

		animals) that were challenged with the anthrax aerosol, NONE survived. Rabbits have also been used to evaluate AVA. 114 (97%) of 117 rabbits vaccinated with AVA survived lethal aerosol challenge, while none of 88 controls survived the challenge. The rabbit, in contrast with the guinea pig, resembles the nonhuman primate in that AVA vaccination confers excellent protection against aerosol challenge.
In March 1997, the FDA warned MBPI that steps would be taken to revoke production licenses, including anthrax vaccine, unless immediate actions were taken to correct longstanding deficiencies. (Pg. 11, par. 1)	The Subcommittee's report leaves out information that would clarify the FDA's intention. DoD supports FDA actions to ensure the quality of vaccine production by MBPI.	The statement in the Subcommittee report left out a sentence, which would have clarified the FDA's intention. Based upon the documented deviations, FDA issued a Notice of Intent to Revoke Letter (NOIR) to MBPI in March 1997. The NOIR letter did not mandate the closure of the facility or lead to seizure of finished product. The letter, however, did state that if MBPI's corrective actions proved to be inadequate, they would run the risk of having their license revoked. MBPI responded to the NOIR with a "Strategic Plan for Compliance" presented to FDA in April 1997.
Vaccine production resumed in May 1999, but neither the renovated facility nor any newly produced vaccine lots have been approved by the FDA. (Pg. 11, par. 1)	BioPort is currently undergoing the normal FDA certification process.	Vaccine must be produced as part of the FDA's process validation. Its use is subject to FDA release. If it is not proven to be potent, sterile safe or effective, it will not be

		used.
In 1992, Secretary of the Army Togo West, Jr. approved a request to indemnify the anthrax vaccine manufacturer, the Michigan Biologics Product Institute (MBPI), against all liability... (Pg. 15, par. 2)	Indemnification of a vaccine manufacturer is for reasons quite similar to those that led Congress to establish the Vaccine Injury Compensation Program (VICP) and is an appropriate, cost-effective method to address potential liability issues for vaccines not covered by the VICP.	The U.S. federal government first indemnified vaccine manufacturers in 1976, to enable production of the swine influenza vaccine that year. Since 1986, the federal government has limited the liability exposure of manufacturers of the most commonly used vaccines in America, primarily those given to children. The Vaccine Injury Compensation Program (VICP) accomplishes this. The 1999 Secretary of the Army memo indemnifies BioPort Corporation for claims arising from administration of anthrax vaccine to service members. Indemnification of BioPort Corporation for potential claims related to anthrax vaccine ensures the availability of anthrax vaccine to protect the nation's Armed Forces against the threat of biological weapons. It does not indicate a lack of faith, confidence or compliance.
…DoD supplemental testing program have raised questions regarding the validity of test procedures and the selection of reference lots. (Pg. 13, par. 1)	There is no problem regarding the validity of test procedures and selection of reference lots.	Additional testing needed to meet the supplemental testing schedule put increased demand on the animal colony resulting in aberrant results and in response. DoD sent a team of external experts to assist BioPort in identifying the cause of these unexpected results. They found the animal colony was too small in number so that smaller animals had to be used for testing which caused the aberrant results. At the same

		time FDA requested BioPort develop a new evaluation method for the potency test. The FDA and BioPort are currently finalizing the approval process for a new evaluation method. It will not reflect a compromise of either quality assurance or compliance with standards.
Following the Gulf War, and prior to adoption of the DoD immunization policy in 1993, and the mandated AVIP in 1998, Pentagon officials considered and rejected alternative anthrax vaccine production sites. Instead, an acquisition strategy was adopted focusing solely on the MBPI/BioPort vaccine. (Pg. 17, par. 1)	Prior to and during Desert Storm/ Desert Shield, DoD investigated the possibility of alternative production sites to meet requirements for a sustained conflict. The conflict resolved before this became necessary.	The process to develop AVA by another manufacturer would require that manufacturer to obtain a FDA license, which would take several years to accomplish. This cannot be accomplished quickly, as it is a very demanding process, negating the immediate or near term use of a second source.
The Army Anthrax Vaccine Immunization Plan directs medical personnel to report severe adverse reactions (resulting in hospitalization or more than 24 hours lost from duty)… (Pg. 19, par. 3)	DoD maintains that the **minimum** reporting would be anyone hospitalized or loss of duty for 24 hours or longer. This does not inhibit others from initiating VAERS reports.	This message has been disseminated in the Policy for Reporting Adverse Events, dated 15 Oct 99 as well as in the educational mediums of the "trifolds', health care providers briefing, leaders briefing and individual briefings.
VAERS guidance recommends recording any clinically significant symptoms occurring subsequent to vaccine administration, whether or not a causal relationship has been established between the vaccine and the adverse reaction. (Pg. 19, par. 3)	DoD continues to address this issue of "clinically significant" symptoms. DoD encourages anyone to submit a Form VAERS-1 no matter what the symptom or temporal relationship.	This message has been disseminated in the Policy for Reporting Adverse Events, dated 15 Oct 99 as well as in the educational mediums of the "trifolds', health care providers briefing, leaders briefing and individual briefings. Members are encouraged to report any symptom they feel could be an adverse reaction.
Once the testing problems became apparent, vaccine lots	All lots have been subjected to supplemented testing. This	After the SecDef's 15 Dec 97 press announcement, DoD

not technically in the stockpile when the AVIP was announced were not subjected to the supplemental assays under the rationale the FDA was requiring the same tests for lot release. All the lots submitted for supplemental testing had also undergone the same FDA lot release protocols. (Pg. 24, par. 3)	testing was established to verify that there were no changes in approved vaccine since FDA certification. It was an extra step to ensure safety.	contracted for 32 lots of the existing vaccine in the stockpile, owned by DoD but stored by BioPort, to be supplementally tested even though they had passed the FDA lot release test. DoD subsequently awarded another, new contract to purchase additional lots of newly manufactured vaccine after MBPI's sale to BioPort in Sep 98. Because these lots still had to be tested and meet FDA lot release criteria, redundant supplemental testing is not necessary and was never contracted.
Without a proven model in animals that is known to correlate to protection in humans, animal data remains only suggestive. (Pg. 25, par. 2)	When a disease is fatal, the use of drug or vaccine animal data is the only way to demonstrate protection in humans. Obviously, it would be unethical to conduct them on humans. In circumstances of this kind, reliance on animal data is necessary and appropriate	"Today, it would be difficult to repeat the efficacy studies because there are no evident populations in the United States where prophylactic vaccine protection could be evaluated in a clinical field trial." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999.* Even according to the testimony prepared by Dr. Nass, "data suggests that the vaccine can protect humans against inhaled anthrax". *Subcommittee on National Security, Veterans Affairs and*

		International Relations Report dated 15 February 2000.
Vaccine-acquired anthrax immunity may also be limited or overwhelmed when the subject is challenged with variant anthrax stains. (Pg. 26, par. 1)	Our vaccine has proven effective against every strain of anthrax against which it has been tested, including the Ames Strain, which is one of, if not the most, lethal strain.	Its use of protective antigen suggests effectiveness against other existing strains as well.
When one U.S. laboratory studying the release of anthrax at Sverdlovsk implied the Russian mixtures of anthrax strains might overcome the protection afforded by the anthrax vaccine, DoD persuaded the author "to correct the press release to make it more accurate. (Pg. 26, par. 5)	The author of the press release corrected the release to make it more accurate after normal scientific discourse with researchers from the US Army Medical Research Institute of Infectious Disease (USAMRIID). It is inaccurate to describe this normal scientific discourse among research professionals as an unethical persuasion.	Scientists from Los Alamos National Laboratory described identification, using gene probes, of multiple strains of anthrax in tissue specimens obtained from victims of the 1979 Sverdlovsk anthrax incident. The laboratory press release implied that mixtures of anthrax strains might overcome the protection afforded by the US anthrax vaccine. After discussions with USAMRIID researchers, the author of the press release, Dr. Walt Kirchner, DoD Programs Office, Los Alamos National Laboratory, agreed to correct the press release to make it more accurate. The modification stated, in part, "…there is no experimental data or evidence to suggest that such a mixture is resistant to the FDA-licensed anthrax vaccine used by the US military."
Hearing testimony and correspondence from Reservists and National Guard members suggests up to 30 percent of some units would resign or seek to transfer due to the anthrax program. (Pg. 28, par. 1)	Admittedly, even one is too many, but there have been no failures of mission accomplishment in any of our units.	"Except in a very small number of cases, Anthrax Vaccination Program is not the determining factor behind a member's decision to withdraw from military service." *Statement by Charles L. Cragin, Principal Deputy Assistant Secretary of Defense for Reserve Affairs, to the Subcommittee on*

		National Security, Veterans Affairs, and International Relations Committee on Government Reform, September 29, 1999. Mr. Cragin also provided a written statement to the Sub-Committee. Many units have retention that is in fact better than the five years prior to implementation of AVIP.
Safety is also an issue for some because the anthrax vaccine is one of the exposures under study by the National Academy of Science's Institute of Medicine (IOM) pursuant to the Persian Gulf War Veterans Act of 1998, enacted as Title XVI of the 1998 Omnibus Appropriations Act, P.L. 105-277. The law directs IOM to review associations between illnesses and wartime exposures that warrant a presumption of service-connection for sick Gulf War veterans. That study is ongoing. (Pg. 28, par. 2)	There is no known link between AVA and Gulf War Illness and no reason to believe one will be found.	When Persian Gulf War veterans returned and started reporting symptoms, some people asked if vaccines administered during the Gulf War might have caused the symptoms. Several independent expert panels addressed this and other questions head-on. These panels consisted of Veterans, civilian academic experts, scientists, health-care professionals, and policy specialists. Each of these panels included some of the nation's best scientists, who spent months or even years listening to veterans, reviewing the evidence, and deliberating the issues. In each case, the independent expert panels found that there was no evidence of any link between any vaccines and any Gulf War illness. To let you read these reports for yourself, hot links appear below. Some of these documents are rather lengthy, so we listed page numbers that refer to vaccines, to speed your

		search. • Presidential Advisory Committee (PAC) on Gulf War Illnesses Final Report, December 1996: p. 114, states: "The committee concludes it is unlikely that health effects reported by Gulf War veterans today are the result of exposure to the botulinum toxoid or anthrax vaccines, used alone or in combination." <http://www.gwvi.ncr.gov/toc-f.html> Pages of Interest: second page, Executive Summary, plus pages 112-114 of the original document (Chapter 4 in the web version). • Health Consequences of Service During the Persian Gulf War: Recommendations for Research and Information Systems, National Academy of Science Institute of Medicine (IOM) 1996: p. 55, 2nd paragraph: concerning adverse interactions due to multiple exposures… "All of these possible drug interactions (and others not mentioned) cause acute and short-term problems. The committee knows of no evidence of any chronic effect." <http://books.nap.edu/books/0309055369/html/1.html> Pages of Interest: 49-

		52, 55, 100. • The Persian Gulf Experience and Health, NIH Technology Assessment Workshop Panel, JAMA, August 3, 1194-Vol 272, No. 5, p.391-395, p. 394, vaccines: general discussion including botulinum and anthrax vaccines…."No long-term adverse effects have been documented." <http://text.nlm.nih.gov/ftrs/tocview/ Select report #14. See the third section, under the caption "Vaccines." • Defense Science Board Task Force on Persian Gulf War Health Effects, June 1994. <http://www.gulflink.osd.mil/dsbrpt/index.html> See chapter VIII, section E.2. • The postwar hospitalization experience of U.S. veterans of the Persian Gulf war. New England Journal of Medicine 1996;335:1505-1513. <http://www.nejm.org/content/1996/0335/0020/1505.asp> This study concluded that "During the two years after the Persian Gulf War, there was no excess of unexplained hospitalization among

		Americans who remained on active duty after serving in that conflict." • The risk of birth defects among children of Persian Gulf war veterans. New England Journal of Medicine 1997;336:1650-1656. <http://www.nejm.org/content/1997/0336/0023/1650.asp> The authors concluded "This analysis found no evidence of an increase in the risk of birth defects among the children of Gulf War veterans." • Mortality among U.S. veterans of the Persian Gulf war. New England Journal of Medicine 1996;335:1498-1504. <http://www.nejm.org/content/1996/0335/0020/1498.asp> The authors concluded: "Among veterans of the Persian Gulf War, there was a significantly higher mortality [death] rate than among veterans deployed elsewhere, but most of the increase was due to accidents rather than disease, a finding consistent with patterns of postwar mortality among veterans of previous wars."
Problems with supplemental testing underscore vaccine safety and production issues. The failure to test all lots	The promise of supplemental testing is being fulfilled on the original stockpile.	The Secretary of Defense ordered supplemental testing of all lots of anthrax vaccine in the Lansing stockpile, when

produced before the plant closed suggests to some the promise of supplemental testing was not fulfilled. (Pg. 29, par. 3)		he authorized the Anthrax Vaccine Immunization Program in December 1997. Supplemental testing repeats the original FDA tests for sterility, purity, potency, and general safety. Supplemental tests are performed by the manufacturer and overseen by an independent contractor (Mitretek, Inc., McLean, Virginia). Supplemental tests are not performed on lots 040 or higher, because these lots were not part of the DoD stockpile in Dec 97, in fact, were not purchased by DoD until after the MBPI sale to BioPort. These newer anthrax vaccine lots have undergone (or will undergo) the same tests for sterility, purity, potency, and general safety required by the FDA to determine whether the lots meet approval criteria for FDA release. Supplemental testing results may be accessed at the AVIP web site: http://www.anthrax.osd.mil/scanned/articles/articles.htm. Supplemental testing problems were identified and corrected with testing resumed on the 32 lots in the original stockpile. *Statement provided by Dr. Robert Myers to the Subcommittee on National Security, Veterans Affairs, and International Relations, April 29, 1999.*

An informal Survey of Reserve and Guard units shows more than 700 current or likely departures due to the AVIP. The survey can be found at: http://www/dallasnw.quik.com/cyberell/Anthrax/Chron_Info.html (Pg. 28, Footnote)	Except for a small number of cases, AVIP is not the determining factor behind a member's decision to withdraw from military service. *Statement by Charles L. Cragin, Principal Deputy Assistant Secretary of Defense for Reserve Affairs, to the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, September 29, 1999.*	Even one serviceman or woman who resigns as a result of not taking a vaccine that was designed to be good for him or her, is one too many. DoD seeks the cooperation of the Congress and the "No Group" to stop encouraging individuals to disobey orders A review of current units who have lost members due to the anthrax vaccine indicate that they are mission capable. There is normally a waiting list to join most units.
Contrary to subsequent DoD characterizations, the promised outside, expert, scientific review of the program was only very general in nature. Others question the necessity of the program, asking whether it betrays a lack of confidence in deterrence and other force protection elements, and suggesting a vaccine program makes anthrax attack more, not less, likely. (Pg. 30, par. 3,4)	DoD reviewed all data prior to Secretary of Defense's announcement to start this program. AVA in conjunction with other force protection elements is used as a deterrent. Vaccination was unanimously recommended by the Joint Chiefs and specifically requested by two Theatre CINCs. We are satisfied with the outside expert scientific review and the credentials of those who participated.	A civilian medical advisory panel to the Food & Drug Administration reviewed all bacterial vaccines in the early 1980s, revoking a few licenses for lack of evidence of safety or efficacy. When that panel considered anthrax vaccine, they reaffirmed all previous NIH and FDA decisions about the vaccine. The report can be found in the 1985 edition of the *Federal Register*, volume 50, pages 51002-117. Second, the Armed Forces Epidemiological Board (AFEB), a civilian body of scientists and physicians, provides recommendations regarding vaccination use and other medical issues to the Assistant Secretary of Defense for Health Affairs (ASD(HA)). AFEB has specific responsibilities in DoD Directive 6205.3, Immunization Program for Biological Warfare Defense.

		The AFEB assists in providing recommendations on vaccines and immunization protocols necessary to enhance protection against validated BW threats. The external Department of Defense Anthrax Vaccine Adverse Event Task Force reviewed adverse events on 3 August 1998 and provided a report on 10 August 1998. The Task Force recommended that reviews of adverse event reports, received as a result of the anthrax immunization program, be performed at 3 to 6 month intervals. Based on a review of the adverse events reported to date and the apparent safety of the anthrax vaccine, the Task Force recommended no other change in the current DoD anthrax immunization program. They also recommended a review of Vaccine Adverse Event Reporting System (VAERS) reports at service level for completeness. AFEB also suggested a small prospective study ("a small records review study") to record all reactions. This led to the survey performed at the Tripler Army Medical Center that involved 603 medical personnel and collected data on symptoms, side effects and reactions subsequent to vaccination. Third, an independent review

		of the health and medical aspects of the program was completed by Dr. Gerard Burrow. Dr Burrow was immensely qualified for this review. He is currently Special Advisor for Health Affairs to the President of Yale University, and he previously served as Dean of the Yale University Institute of Medicine, Vice Chancellor for Health Services of the University of California (San Diego), Dean of the School of Medicine of the University of California (San Diego), and Member of the Institute of Medicine, National Academy of Sciences. He completed his review on 19 February 1998. Fourth, the Anthrax Vaccine Expert Committee (AVEC) is a panel of civilian physicians convened by the Health Resources & Services Administration of the Department of Health & Human Services to review all VAERS reports submitted to the FDA. This independent external review panel meets every 6 weeks or so. To date, the committee has identified no unexpected events after anthrax vaccination. Today, there is a broad consensus that the FDA-licensed anthrax vaccine is safe and effective for people at high risk of exposure. Recent publications of the CDC [ftp://ftp.cdc.gov/pub/

		Publications/mmwr/wk/mm4804.pdf] and the Johns Hopkins Center for Civilian Biodefense Studies [http://www.ama-assn.org/sci-pubs/journals/archive/jama/vol_281/no_18/jst80027.htm] recognize the anthrax vaccine as part of the national preparedness against biological terrorism. Anthrax vaccination is needed because the threat is real and lethal. The Chairman of the Joint Chiefs of Staff named anthrax as the #1 biological threat. The current world threat environment and the unpredictable nature of terrorism make it prudent to include biological warfare defense as part of our force protection planning. Weapons inspectors discovered during the Gulf War that Saddam Hussein maintained an anthrax arsenal sufficient to kill every man, woman and child on the face of the earth. By 1992, U.S. intelligence sources recognized that the former Soviet Union maintained a capability that dwarfed Iraq's. Inhalation anthrax following a biological warfare attack is almost invariably lethal to those who become infected, if not treated quickly. Even with prompt treatment, the likelihood of death is 80%. Bio-weapon attacks would probably not be detected until large numbers of people

		become ill. The anthrax vaccination program is a critical component of DoD's multi-component Force Health Protection Strategy to protect the force from the threat of this bio-weapon.
Some who testified are experiencing serious illnesses they associate with the anthrax vaccine. (Pg. 31, par. 2)	While the overwhelming majority of reactions will be minor, the Department is aware that serious reactions are a possibility. Because of that possibility, each service member who reports an illness subsequent to a dose of this vaccine, or any other, is evaluated and treated for his or her illness or symptom. Some of those testifying were later found to have had pre-existing medical conditions vice reactions. Some are still under study.	The Anthrax Vaccine Expert Committee (AVEC) is a panel of civilian physicians convened by the Health Resources & Services Administration of the Department of Health & Human Services to review all VAERS reports submitted to the FDA. This independent external review panel meets every 6 weeks or so. To date, the committee has identified no unexpected events after anthrax vaccination. There are many more individuals who have taken the AVA without any reactions. These individuals were not asked to provide statements to the Subcommittee. Over 1.4 million shots have been given to over 400,000 personnel. Reactions reported to date are below those of almost all other vacciness.
Entitled, "Anthrax Vaccine Adverse Reactions," the hearing focused on the program's willingness to recognize and ability to treat adverse reactions to the vaccine in military personnel. Issues discussed included the	Recognizing that this is the largest use of AVA, a safety program was designed by DoD and articulated during the multiple Subcommittee hearings. DoD medical professionals are	The DoD Safety program was described in detail during testimony to the Subcommittee on National Security, Veterans Affairs and International Relations. None of this testimony was reflected in the Subcommittee's report.

extent the main adverse event surveillance system used by DoD, the joint FDA/CDC Vaccine Adverse Event Reporting System (VAERS), under-reports adverse events and adverse vaccine reactions. (Pg. 31, par. 4)	well trained and are capable of treating adverse events presented by service members for a multitude of reasons.	As reported by Major General Claypool, "DoD conducts an aggressive, multi-faceted surveillance program to assess vaccine safety. In fact, the safeguards of vaccine administered to DoD personnel meets or exceed every standard for vaccine administration to the civilian population. The DoD program uses three scientific methods to evaluate safety, clinical studies, database studies and spontaneous reports (passive surveillance). The extent of this safety surveillance far exceeds any vaccine program in the United States for both childhood and adult vaccines."
Rep. Walter Jones (NC) introduced HR 2543 on July 16, 1999. Entitled "The American Military Health Protection Act," the bill would instruct the DoD to make the anthrax military vaccination immunization program voluntary for all members of the Armed Forces until the FDA has approved a new anthrax vaccine for humans or the FDA has approved a new, reduced course of shots for the current anthrax vaccine. This bill was referred to the Committee on Armed Services. (Pg. 32, par. 4)	DoD opposes having the vaccinations voluntary.	It could leave part of our force unprotected and result in mass casualties. It would also interrupt the established FDA protocol for any participating service member who elected not to continue the protocol.
The FY2000 Defense Appropriations Act (HR 2561) contained a provision directing the Comptroller General to report on: effects on morale, retention and	This is correct and action is ongoing to meet the Act's provisions.	DoD will fully cooperate and looks forward to the results of these new studies. We believe these studies will validate the many studies which have already done and will support

recruiting; the civilian costs and burdens associated with adverse reactions for members of the reserve components; adequacy of long and short term health monitoring; assessment of the anthrax threat, including but not limited to foreign doctrine, weaponization, quality of intelligence, and other biological threats. DoD was directed to contract with the National Research Council to conduct studies on: vaccine adverse events and adverse reactions, particularly among women; vaccine efficacy against inhalation anthrax; correlation of animal models to safety and efficacy in humans; research gaps; and other matters. (Pg. 32, par. 6)		our ongoing efforts.
AVIP represents a doctrinal departure overemphasizing the role of pre-exposure medical intervention in force protection. (Pg. 34, par. 1)	DoD utilizes vaccines as pre-exposure for prevention of all types of disease that service members may encounter during deployment.	Vaccination is a cornerstone to fighting disease in the United States. A major difference between this and other mandatory vaccines is that the decision to begin the series came late in our careers as opposed to being given in initial training. There are several mandatory vaccines.
But in the absence of proven capability and intent to use biological weapons, vulnerability alone does not constitute a validated threat for purposes of determining appropriate and effective countermeasures. (Pg. 22, par. 3)	DoD has determined that there is a valid threat. CIA and DIA agree. Even the Subcommittee's report mentions that clearly there is a real and imminent threat.	There is some evidence that anthrax was used as a biological weapon (BW) on a limited basis by the Japanese in China during World War II (Christopher GW, et al. Biological warfare: A historical perspective. *JAMA* 1997; 278(Aug 6): 412-17). Since then, several countries are believed to have incorporated anthrax into

		biological weapons. Intelligence analysts believe that at least seven potential adversaries have an offensive BW capability to deliver anthrax - twice the number of countries compared to when the 1972 Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Construction (commonly called the Biological Weapons Convention) took effect. The Biological Weapons Convention was designed to prohibit such activity. Iraq admitted to the United Nations in 1995 that it loaded anthrax spores into warheads during the Gulf War. In the post-cold war era, the former Soviet Union admitted to having enough anthrax on hand to kill every person on the planet several times over. The accidental aerosolized release of anthrax spores from a military microbiology facility in Sverdlovsk in the former Soviet Union in 1979 resulted in at least 79 cases of anthrax infection and 68 deaths and demonstrated the lethal potential of anthrax aerosols.
So the threat remains tactically limited and regional. The AVIP is universal. (Pg. 39, par. 3)	Conflicts have traditionally been regional not global. Worldwide deployability of all forces, active and reserve component, mandates universal vaccination with the	The following concept is expressed in the instructions entitled, Joint Instruction, Immunizations and Chemoprophylaxis, AFJI 48-110, AR 40-562,

	anthrax vaccine.	BUMEDINST 6230.15, and CG COMDTINST M6230.4E: Current health threat assessments based on disease prevalence in specific geographic regions are maintained by each Service preventive medicine authority using federal, DoD, and other relevant sources of information and are disseminated appropriately to all units within their respective jurisdictions. Specific immunization requirements are based on special disease threat assessment. Full protection against anthrax is afforded only after the 6 doses are administered over 18 months, so anthrax vaccination must begin now to protect our forces in the future and to prepare members who will be rotating through the units.
That study was conducted, for the most part, behind closed doors. However, the documentation provided to the subcommittee by DoD describes a process more predetermined than deliberative, as the obvious operational benefits of passive, pre-exposure protection … (Pg. 40, par. 1)	DoD undertook a detailed, deliberative process over more than three years that culminated in the decision to implement a mandatory, force-wide AVIP.	This was conducted in the normal business processes that DoD uses to determine decisions and policy. It included input and research from medical, scientific, university research laboratory and many other activities. DoD believes that if members of the Committee and Subcommittee had conducted the same research that we had, they would agree with the program we have implemented.
The mission profile for the improved vaccine called only	This statement in the Subcommittee report was	Conceptually, a new anthrax vaccine could provide

for inoculation of deployed and rapid deployment units based on intelligence estimates of the potential for use of specific BW agents against U.S. forces. ... Other military personnel will be vaccinated prior to departure to BW threat areas. An accelerated immunization program will be conducted under certain alert or mobilization conditions. (Pg. 41, par. 3)	lifted from a DoD "Operational Requirements Document (ORD) for Improved Anthrax Vaccine"; report dated 2 Oct 1995. It was an evolving step to an evolving threat.	protection after only a single dose. If this were true, this new vaccine could be administered like other vaccines DoD administers, just prior to deployment to forces at risk. This has no bearing on the current AVIP which uses the currently FDA licensed vaccine requiring 6 doses given over 18 months for full protection.
Shortcomings of the currently licensed vaccine were seen as the "serious logistical obstacles, especially for reserve force "posed by the approved six-shot schedule and reports that suggest "this vaccine may not provide universal protection against all anthrax strains." (Pg. 41, par. 4)	DoD recognizes that the FDA approved dosing schedule represents a challenge. To this end, we mandated use of automated immunization tracking systems to manage the program. For Reserve Component (RC) forces in particular, DoD established several initiatives through the Public Health Service, the VA, and a private sector contract to increase access for vaccination and treatment. DoD believes that the current anthrax vaccine would be effective against all strains of anthrax because of its incorporation of protective antigen.	DoD now maintains agreements with the Division of Federal Occupational Health, Public Health Service; the Department of Veterans Affairs; and Arora Group, Inc to provide vaccinations and treatment to military personnel through a preferred provider network at more than 12,000 locations throughout the US. This greatly facilitates RC adherence to the dosing schedule. The current U.S. licensed anthrax vaccine is considered to be highly effective against naturally occurring strains of anthrax, including antibiotic-resistant strains. This is because anthrax vaccine targets the key disease-causing protein common to all strains of anthrax. DoD is aware of the Russian research effort recently reported in a British scientific journal. Russian scientists reported using technology to introduce two foreign genes

		into anthrax. The potential for a genetically altered virulent organism is of concern to us and we are anxious to learn more about this organism. Hamsters, vaccinated with the Russian live attenuated anthrax vaccine were not resistant to challenge with their engineered strain. There are substantive scientific questions about this report. First, the validity of the animal model that the Russians used needs to be addressed, because hamsters may not be predictive of results in other animals and humans. Second, the strain produced may not be stable, a fact the Russians admit. An unstable organism would not be a candidate for weaponization. There have been ongoing efforts by OSD Cooperative Threat Reduction Program, the National Academy of Sciences, and the International Science and Technology Center to evaluate the possibility of a potential threat from genetically modified strains, and to ensure that our vaccine is effective against them. We believe that the current anthrax vaccine would be effective against altered genetic strains based on the biologic principles of the U.S. vaccine, which is different from the Russian vaccine.
Briefing materials produced by the U.S. Army Medical Research Institute of	During the normal course of DoD decision-making, all pros and cons are assessed,	Concurrent with the AVIP using the currently FDA-licensed anthrax vaccine, DoD

Infectious Disease (USAMRIID) in 1994 listed the following problems with the current vaccine: Prolonged immunization schedule Reactogenicity: Systemic reactions: .7 - 1.3% Significant local reactions: 2.4 -3.9% (5.9%) Vaccine components completely undefined in terms of characterization and quantitation of the PA, and other bacterial products and constituents present Significant lot-to-lot variation in the PA immunogen content Human trials with similar but not identical vaccine showed protection against cutaneous anthrax but insufficient data to show efficacy against inhalation anthrax Made from spore-forming strain requiring dedicated production facility. (Pg. 41, par. 5)	evaluated, and debated. The DoD decision to implement the AVIP considered all these factors.	is pursuing research to produce a new anthrax vaccine using recombinant technology that hopefully will result in fewer required doses and fewer side effects than the currently licensed product. This is responsible pursuit of better medicine technology. It does not, however, exist today. Unfortunately, the threat does exist. It would be irresponsible not to use the available protection - an FDA licensed and approved, safe and effective vaccine.
At the same time, DoD interest in an improved anthrax vaccine diminished sharply. Reservations about the suitability of the old vaccine were put aside once it was made the centerpiece of the proposed immunization effort. (Pg. 42, par. 6)	DoD does not have reservations concerning the suitability of anthrax vaccine adsorbed and it has not kept us from pursuing a better vaccine for the future.	"In completing an Industrial Capabilities Assessment, it was determined that while a series of alternatives were available, only two options were realistic in meeting DoD's requirement: 1) Seek alternative manufacturing sources and 2) maintain current capability… the only viable alternative that will support the current policy of total force vaccination is to continue with the current manufacturer. In evaluating the industrial base in the

		biological defense area, DoD found little interest by U.S. commercial firms." *Statement by Honorable John J. Hamre, Deputy Secretary of Defense to Subcommittee on Military Personnel House Committee on Armed Services, First Session, 106th Congress, 30 September, 1999.* None of Mr. Hamre's statement was included in the subcommittee's report. Concurrent with AVIP using the currently FDA-licensed anthrax vaccine, DoD is pursuing research to produce a new anthrax vaccine using recombinant technology that hopefully will result in fewer required doses and fewer side effects than the currently licensed product.
One statement of chem/bio defense doctrine ranks force protection strategies as follows: "... The most effective and singularly most important prophylaxis in defense against biological warfare agents is physical protection. Preventing exposure of the respiratory tract and mucous membranes ... to infectious and/or toxic aerosols through use of a full-face respirator will prevent exposure, and should, theoretically, obviate the need for additional measures. Chemical protective masks effectively filter biological hazards. ... All medical	DoD policy maintains vaccination, as disease prevention, is but one pillar of force protection. At this point in time, it is the best protection available.	The first protection we rely on is deterrence. We hope it is successful, but we know it will not always work. Next we rely on intelligence and hope to thwart the attack before it occurs. Our intelligence is not perfect. We cannot always count on it. We have good protective clothing, but we cannot wear it 24 hours a day and cannot fight in it for long periods of time. We have detectors and warning devices, but we only have a few and they are early state-of-the-art. The best and most effective piece of the Bio-Protection suite is our FDA licensed, safe and effective vaccine.

prophylactic modalities described should be viewed only as **secondary** (i.e. backup), and are not to be relied upon as primary protective measures. Agent exposures near the source of dissemination will be high, and likely to overwhelm any medical protective measure." The AVIP makes medical prophylaxis is a primary aspect of force protection and CBW deterrence. (Pg. 44, par. 1)		The vaccine would protect our servicemen and women in the instance of an unannounced, undetected release of anthrax aerosol. The aerosol is tasteless, odorless and invisible and could infect our forces at a time when they are not wearing protective gear.
The vaccine policy also reflects a lack of confidence in current force protection equipment. (Pg. 46, par. 5)	DoD uses vaccination as one prong in the policy of force protection. Our mask, suits and detectors continue to be improved.	Early warning detection equipment is in its developmental stages. Service members would be unable to wear protective gear twenty-four hours a day, seven days a week. This leaves service members vulnerable to attacks with biological agents and points to the need for vaccination as a prong of force protection. Use of the vaccine provides an avenue of protection that more gear and intelligence cannot provide in an unannounced silent attack.
Even this doctrinal reliance on the primacy of medical protection does not necessarily demand the universal, pre-deployment inoculation that characterizes the AVIP. (Pg. 48, par. 1)	Deployment possibilities are worldwide and **do** require universal vaccination.	Many vaccinations, for example hepatitis A, are given universally to service members during basic training to prepare them for worldwide deployment.
Other inoculations are required pursuant to medical, not military command authority, and they are required primarily to maintain and protect the health of	The Armed Forces Epidemiology Board (AFEB) recommends vaccinations that are necessary for force health protection in the DoD.	Medicine is a support function for the line units. Anthrax shots are as safe and effective as other vaccines and are accompanied by

personnel from naturally occurring diseases or pathogens endemic to specific duty or deployment areas. (Pg. 50, par. 1)		comparable adverse reactions.
Although the threat of natural anthrax "remains a significant problem in numerous countries throughout Africa, the Middle East, Europe and Asia," the general military immunization policy contains no reference to the anthrax vaccine. (Pg. 50, par. 1)	DoD policy is currently being revised to include anthrax vaccine. It just wasn't part of our program when the policy was last published.	The following concept is expressed in the instructions entitled, Joint Instruction, Immunizations and Chemoprophylaxis, AFJI 48-110, AR 40-562, BUMEDINST 6230.15, and CG COMDTINST M6230.4E, dated Nov 1995: Current health threat assessments based on disease prevalence in specific geographic regions are maintained by each Service preventive medicine authority using Federal, DoD, and other relevant sources of information and are disseminated appropriately to all units within their respective jurisdictions. Specific immunization requirements are based on special disease threat assessment. The 1995 policy included FDA licensed vaccines for endemic diseases worldwide. No vaccines for bio-warfare were listed or in use at that time.
"Deploying civilian employees who decline to participate in the DTRA-AVIP will be required to execute a "Statement of Informed Declination" attesting to the Agency's offer of anthrax immunization and the individual's decision to decline. (Pg. 50, par. 4)	The Defense Threat Reduction Agency rescinded this policy.	Emergency-Essential civilians and contractors who perform mission essential services are part of our war-fighting team and as such are expected to take the vaccine when deploying with our forces. The applicable documents include the following: - DoD Directive Number

		1404.10, April 10, 1992, Emergency-Essential (E-E) DoD U.S. Citizen Civilian Employees. - DoD Instruction Number 3020.37, November 6, 1990, Continuation of Essential DoD Contractor Services During Crises.
DoD concluded, but cannot prove, that individual antibody response to the vaccine equals protection from anthrax attack. (Pg. 50, par. 5)	Vaccine is known to be safe and effective against anthrax. This is not just a DoD opinion.	"The only known effective prevention against anthrax is the anthrax vaccine. Treatment of cutaneous anthrax infection involves administration of antibiotics. In the case of pulmonary anthrax infection, therapy has been of limited benefit, except when given immediately after exposure." *Statement by Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives, April 29, 1999* Antibiotics must be given before symptoms develop to be effective. Since the spores are colorless, odorless and tasteless, normally one would not know they had been exposed until symptoms developed. <u>Animal studies</u>: – In support of the clinical studies, two

		rabbit animal protocols were completed to develop an in vitro correlate of immunity in a relevant animal model. These studies also accomplished a comparative pathology evaluation between rabbit and non-human primate models. References: (1) Protocol Number F96-17. Development of an in vitro correlate of immunity for anthrax in the rabbit model (2) Protocol Number F97-08. Confirmation of an in vitro correlate of immunity for anthrax in the rabbit model using AVA Lot FAV032. In the nonhuman primate studies, a total of 62 (94%) of the 65 animals vaccinated with AVA survived a highly lethal challenge of aerosolized anthrax. Whereas, of the 18 controls (unvaccinated animals) that were challenged with the anthrax aerosol, NONE survived. Rabbits have also been used to evaluate AVA. 114 (97%) of 117 rabbits vaccinated with AVA survived lethal aerosol challenge, while none of 88 controls survived the challenge. The rabbit, in contrast with the guinea pig, resembles the nonhuman primate in that AVA vaccination confers excellent protection against

		aerosol challenge.
Nevertheless, DoD concludes enrollment in the AVIP equals protection for purposes of satisfying the need for uniform force protection. (Pg. 52, par. 1)	DoD policy is to follow the approved FDA dosing schedule to gain the proven protection needed.	Numerous studies support this finding. No studies disprove it.
In tactical terms, the protection afforded by vaccination would be needed only during the time between detection and the order to deploy individual and collective physical protective measures (suits, masks, tents, etc.). Better detection capability, improved masks and a battlefield doctrine to deploy protective measures earlier could limit or eliminate the need even for that small window of protection provided by the vaccine. (Pg. 52, par. 2)	DoD utilizes vaccines as pre-exposure prevention of many types of disease that Service Members may encounter during deployment.	Vaccination is a cornerstone to fighting disease in the United States and has been for many years. The anthrax attack that would endanger our members would be disseminated in a manner to best utilize its colorless, odorless, tasteless and difficult-to-detect character. Therefore, it is not guaranteed that members will be afforded the opportunity to use the physical protective measures available to them. "Post-exposure vaccination following a biological attack with anthrax [vaccine] would be recommended with antibiotic administration to protect against residual retained spores…" *Journal of the American Medical Association, May 12, 1999, Vol. 281, No. 18, p 1740.* Such treatment is helpful if given within 24-48 hours of exposure, and prior to the development of symptoms. Once a member becomes symptomatic, however, such treatment would likely be too late and not be lifesaving.
The sole-source procurement of a vaccine that requires a dedicated production facility	BioPort Corporation renovated and modernized the AVA production suite and now is	The anthrax vaccine works. No one who has taken the vaccine is known to have

leaves DoD captive to old technology and a single, untested company. (Pg. 53, par. 1)	involved in the normal process of FDA certification under a Biologics License Application (BLA).	contracted inhalational anthrax; Whether one considers it old or current, the vaccine is effective. The new BioPort facility is one of the more modern of its kind in the country.
Research and development on a second-generation, recombinant vaccine would allow others to compete. (Part 53, par. 1)	This may be true, but it would be years away, and the threat is now. We are pursuing the second-generation vaccine as well.	"In completing an Industrial Capabilities Assessment, it was determined that while a series of alternatives were available, only two options were realistic in meeting DoD's requirement. 1) Seek alternative manufacturing sources and 2) maintain current capability…the only viable alternative that will support the current policy of total force vaccination is to continue with the current manufacturer. In evaluating the industrial base in the biological defense area, DoD found little interest by U.S. commercial firms." *Statement by Honorable John J. Hamre, Deputy Secretary of Defense to Subcommittee on Military Personnel House Committee on Armed Services, First Session, 106th Congress, 30 September, 1999.* None of Mr. Hamre's statement was included in the subcommittee's report.
DoD has built a force-wide program on the narrowest possible industrial base. (Pg. 53, par. 2)	The same is true for most other vaccines. However, a second source will be pursued.	Such a solution is months to years away, while the threat is real now.
FDA inspection findings on the renovated facility contain a number of observations repeated from the February 1998 inspection. (Pg. 55, par.	BioPort Corporation renovated the AVA production suite and is now involved in the normal process of FDA certification under a Biologics License	"The February 1998 inspection disclosed deviations from FDA's regulations. These deviations included, but were not limited

1) GAO also found the dependent relationship between DoD and BioPort unusual and risky. While sole-source procurements for vaccines may be common, those producers usually have other product lines generating income from other customers. (Pg. 59, par. 1) One vaccine producer operating a single production site also points to security risks. (Pg. 59, par. 2) GAO observed, "But if we are relying upon this vaccine as part of the backbone of our defensive biological program, the question of vulnerability to a single site becomes an issue. If you made a decision with respect to that vulnerability that led you to want to have an alternative site, then we probably should be looking at establishing a second source." (Pg. 59, par. 2)	Application (BLA).	to, the manufacture of the anthrax vaccine. In addition, the inspection resulted in a request by FDA that MBPI quarantine 11 lots of anthrax vaccine held in storage, pending review of additional information to be submitted by BioPort… These lots are still in quarantine, and will remain in quarantine until the company submits required information to the Agency. FDA noted that MBPI had made progress in achieving its compliance goals, but additional work remains in order to correct the deviations related to the manufacture of the anthrax vaccine. Pursuant to its purchase of the MBPI facility in September 1998, BioPort agreed to abide by the strategic plan and other commitments for corrective actions made by the management of MBPI. It should be noted that MBPI halted production of anthrax vaccine sublots in January 1998 to begin a comprehensive renovation of the anthrax production facilities." *Kathryn C. Zoon, Ph.D. Director, Center for Biologics Evaluation and Research, Food and Drug Administration, Department of Health and Human Services Before the Subcommittee on National Security, Veterans Affairs, and International Relations Committee on Government Reform, U.S. House of Representatives,*

		April 29, 1999 As previously stated, a second source will be pursued, however, this cannot be accomplished immediately. BioPort Corporation also produces Diphtheria-Tetanus (DT) Pediatrics, Rabies Vaccine Adsorbed, Immune Globulin (Human), as well as Albumin (Human), which target domestic and international markets.
Rather than risk long term health impairment, some service members would be willing to consider the vaccine-preventable risk of anthrax among the inherent, unavoidable risks of military service. They do not have that option, an opportunity to assume risk made available to essential civilian employees of the Defense Threat Reduction Agency. (Pg. 97, par. 3)	The DTRA agency policy was rescinded. All DoD immunizations are mandatory.	If an FDA certified, safe and effective protective vaccine did not exist, such a choice might be prudent. Given the availability of safe and effective protection, it would be highly irresponsible to send troops into battle without it.
Others view this force protection effort as an untested medical solution to a purely mechanical problem - contamination prevention and avoidance - better solved by physical rather than pharmacological technology. (Pg. 97, par. 4)	DoD uses vaccination as one prong in the policy of force protection.	Early warning detection equipment is in its developmental stages. Service members would be unable to wear protective gear twenty-four hours a day, seven days a week. This leaves service members vulnerable to attacks with biological agents and points to the need for vaccination as a prong of force protection.
But DoD is unwilling to wait for the research, development and FDA approval processes, even though DoD believes within a year we will get FDA approval for reduced dose	The threat of this biological agent is now; therefore, DoD has an urgent need to protect the force now and cannot wait for the reduced dose study, which will take at least a year	DoD will make the appropriate changes to the AVIP, if and when the FDA approves changes to the licensed dose schedule and vaccination route, subsequent

based on the science. (Pg. 100, par. 3)	or two to complete.	to the completion of the necessary clinical studies.
To address the domestic bioterrorism threat, the Department of Health and Human Services' National Institute of Allergy and Infectious Diseases formed a working group to develop and test a second-generation anthrax vaccine, and the Institute has funded some research. DoD should support those efforts. (Pg. 100, par. 4)	DoD works with and does actively support the DHHS in this endeavor.	DoD is participating in and will be anxious to have the results of this effort.
With regard to an improved anthrax vaccine, the American Public Health Association adopted a policy statement in November 1999 urging DoD to "delay any further immunization against anthrax using the current vaccine or at least to make immunization voluntary" and to convene a commission of military and non-military public health experts to review safety and efficacy evidence for the current vaccine, attempt to determine when an improved vaccine might be available, and make recommendations about continuation of the current program. (Pg. 101, par. 1)	DoD Force Health Protection cannot effectively be a voluntary program, and the threat is now.	The APHA policy was adopted after a presentation that only covered the opposing viewpoint. DoD offered to present our views and findings but the offer was declined. Adopting a policy after hearing only one side of an issue is inappropriate.
DoD expended significant time and resources in 1994 and 1995 on plans and programs to demonstrate the safety and efficacy of a shorter anthrax inoculation regime, and a different route of administration, but appears to have all but abandoned those efforts when planning for the AVIP began. Support for the	DoD and the manufacturer pursued this research in the past and continue this effort now.	The Comparative Study to Determine the Best Two-Dose Schedule and Route of Administration of Human Anthrax Vaccine, by Dr. Phillip Pittman, sponsored by Dr. Robert Myers, MBPI (now BioPort) was submitted to the FDA in Fall 1998. The results were favorable but the FDA requires a larger pivotal

FDA application to reduce the shot course seems to have been redirected to vaccine acquisition and AVIP logistics. (Pg. 105, par. 1)		study. Funding has been obtained and DoD is working in conjunction with the CDC, NIH and the sponsor (BioPort) to complete this study.
"In November 1971, the Division of Biologics Standards, NIH, noted an apparent increase in reports of adverse reactions after individuals received booster shots. The Division considered it advisable to reevaluate the need for annual boosters and possibly the amount of the booster dose. Although the record is unclear as to whether or not NIH requested a reevaluation, to date, no such reevaluation has been done." (Pg. 102, par. 5)	A study of immunogenicity is currently being conducted under CDC oversight.	DoD will anxiously await these results.
For this purpose, "suitable" should not just mean FDA approved, but demonstrably as safe and effective as possible for the intended military use. A vaccine that takes 18 months, and annual boosters, to confer immunity should not be considered suitable under the policy. (Pg. 103, par. 1)	DoD disagrees given the threat.	FDA is Congressionally charged with the mission of approving for licensure only those drugs, vaccines and devices that are safe and effective and thus suitable for human use.
In terms of increased safety, there is also some evidence an intravenous injection would produce fewer side effects and adverse reactions than subcutaneous administration. (Pg. 104, par. 5) (emphasis added)	The term *intravenous* is incorrectly used in this sentence: the correct term is intramuscular. In the past, the DoD and the manufacturer have pursued research on using alternate routes of administration and continue in this research effort now.	The Comparative Study to Determine the Best Two-Dose Schedule and Route of Administration of Human Anthrax Vaccine, by Dr. Phillip Pittman, sponsored by Dr. Robert Myers, MBPI (now BioPort) was submitted to the FDA in Fall 1998. The results were favorable but the FDA requires a larger pivotal study. Funding has been obtained and DoD is working in conjunction with the CDC,

		NIH and the sponsor (BioPort) to complete this study.
DoD only recently began "to design a set of studies to better evaluate the long term safety of the anthrax vaccine ... to conform with present-day, post-marketing practice" (Pg. 106, par. 2)	In 1970 when the vaccine was licensed, the FDA did not require post-marketing studies. FDA changed this requirement to improve product information and safety. This said, there exists more long-term safety data on the anthrax vaccine than many other vaccines currently routinely administered to populations in the U.S., such as hepatitis A and B and chicken pox (varicella).	To date, at least 12 human studies have assessed the safety of anthrax vaccination. These studies, some stretching back almost 50 years, reported adverse events after vaccination, in varying degrees of detail. The following paragraphs list the studies. Among the studies listed below, one of two vaccine formulations was used. The Brachman study and the early Fort Detrick studies used anthrax vaccine manufactured according to the original 1950s formula developed at Fort Detrick, Maryland. In the 1960s, the production process for anthrax vaccine was improved to increase the concentration of the active ingredient, protective antigen, (thus increasing the vaccine's potency) and to decrease the amount of other bacterial components in the vaccine (thus increasing purity). This purer, more potent vaccine, manufactured in Lansing, Michigan, was licensed by the FDA in 1970. The CDC observational study involved people who received either the original vaccine or the improved vaccine, or both. The other studies described below used anthrax vaccine manufactured according to the improved 1960s formula, the

		same vaccine used throughout the United States today. Details of each study appear on following pages. The twelve studies include: a. The Brachman Study (the pivotal field trial evaluating the safety and efficacy of anthrax vaccination). b. The CDC Observational Study (the follow-on study between the Brachman Study and vaccine licensing in 1970). c. The Fort Detrick Multi-Dose, Multi-Vaccine Safety Studies (evaluations of Army laboratory workers vaccinated hundreds of times with dozens of vaccines). d. The Fort Detrick Special Immunization Program (SIP) Safety Study (a continuation of the previous study among more workers into modern times). e. The Fort Bragg Booster Study (an evaluation of additional doses of anthrax vaccine among soldiers vaccinated several years earlier during the Persian Gulf War). f. The USAMRIID Reduced-Dose / Route-Change Study (a study of anthrax vaccine administered by two different injectable routes of administration).

		g. The Canadian Forces Safety Survey (a study of Canadian Service Members). h. The TAMC-600 Survey (a study of adverse events after anthrax vaccination of medical personnel at Tripler Army Medical Center). i. The U.S. Forces Korea Records Study (a study of adverse events among service members serving in Korea). j. The USAF Vision Study (a study of visual acuity among vaccinated and unvaccinated aircrew members). k. The USAF Air Combat Command Study, Langley Air Force Base (a study of outpatient medical care among Air Force personnel after return from Southwest Asia). l. The reports involving Anthrax Vaccine submitted to the FDA/CDC Vaccine Adverse Event Reporting System (VAERS). SUMMARY: Like all vaccines, anthrax vaccine may cause soreness, redness, itching, swelling, and lumps (a subcutaneous nodule) at the injection site. About 30% of men and 60% of women report mild local reactions, but these reactions usually last only a few days. Lumps can persist for a few weeks, but

		eventually completely resolve. For both genders, between 1% and 5% report moderate reactions of 1 to 5 inches in diameter. Larger reactions occur after about one in a hundred vaccinees or less. Beyond the injection site, from 5% to 35% will notice muscle aches, joint aches, chills, fever, headaches, nausea, loss of appetite, malaise, or related symptoms. Again, these symptoms usually go away after a few days. To monitor rare or unexpected adverse events associated in time to any vaccine, DoD health care providers have participated in the Vaccine Adverse Event Reporting System (VAERS) since its inception in 1990, when it was established by the Department of Health and Human Services. In addition, each VAERS report is reviewed by an independent panel of civilian physicians. To date, this panel has detected no patterns of unexpected adverse events related to anthrax vaccination. There are no known long-term patterns of side effects from the anthrax vaccine, based on an ongoing series of studies at Fort Detrick, Maryland, and elsewhere. The first report in this series was published in 1958. Despite the extensive body of

		knowledge regarding the safety of anthrax vaccine, safety monitoring continues, as is prudent for all vaccines and medications.
Therefore,"a member of the Reserve Component may present themselves for initial treatment and evaluation at any military treatment facility, after vaccination during a period of duty. The member will be examined and provided necessary medical care. Once treatment is rendered or the individual's emergent condition is stabilized a Line of Duty and/or Notice of Eligibility status will be determined by the member's unit, as required. No treatment beyond that justified to stabilize the condition or emergency is authorized until Service connection is validated." (Pg. 106, par. 4)	Adverse events linked to DoD-directed immunizations are treated the same as any other line of duty injury or illness per Title 10, United States Code for the Armed Forces.	*Office of the Assistant Secretary of Defense for Health Affairs memorandum subject: Ensuring Reserve Component Have Full Access to Department of Defense (DoD) Military Treatment Facilities (MTF) for Treatment Evaluation of Adverse Events from DoD Directed Immunizations, dated 20 Jul 1999, states:* "Title 10, United States Code for the Armed Forces directs that members of the Reserve components who incur or aggravate any injury, illness, or disease while performing active duty for less than 30 days, or inactive duty training are entitled to medical care appropriate for the treatment of the injury, illness or disease. Adverse reactions from DoD-directed immunizations are line of duty illnesses. Therefore, when a member of the Reserve component presents for treatment at an MTF, expressing a belief that the condition for which treatment is sought is related to receiving an immunization during a period of duty, the member must be examined and provided necessary medical care." The Department has initiated a network of health care

		facilities to support Reserve Component (RC) personnel, not only for anthrax vaccination and/or vaccine-related reactions, but also for medical care.
But requiring an immediate determination of service-connection for vaccine related health effects means many short term, and most long term, adverse reactions will not be monitored by DoD physicians. (Pg. 107, par. 1)	Line of Duty and/or Notice of Eligibility will be determined as soon as possible. Commanders initiate the investigation process once he/she has been notified by the service member.	*Office of the Assistant Secretary of Defense for Health Affairs memorandum subject: Ensuring Reserve Component Have Full Access to Department of Defense (DoD) Military Treatment Facilities (MTF) for Treatment Evaluation of Adverse Events from DoD Directed Immunizations, dated 20 Jul 1999, states:* "Title 10, United States Code for the Armed Forces directs that members of the Reserve components who incur or aggravate any injury, illness, or disease while performing active duty for less than 30 days, or inactive duty training are entitled to medical care appropriate for the treatment of the injury, illness or disease. Adverse reactions from DoD-directed immunizations are line of duty illnesses. Therefore, when a member of the Reserve component presents for treatment at an MTF, expressing a belief that the condition for which treatment is sought is related to receiving an immunization during a period of duty, the member must be examined and provided necessary medical care."
Enrollment of every vaccine recipient in a clinical	Enrollment of 2.4 million people in a comprehensive	Through its automated immunization tracking

evaluation and treatment protocol would allow DoD to capture a unique and valuable data set for use in their longitudinal studies, avoiding disputes over cohort selection bias and other methodological issues. (Pg. 107, par. 2)	treatment protocol is not warranted by the adverse reaction data collected and evaluated to date. Neither the FDA, CDC, AVEC, nor the Longitudinal Studies Concept Committee have found any adverse events, not otherwise expected, nor have made a recommendation for such an evaluation and treatment protocol. Such a protocol at this time is neither standard medical practice, recommended, or cost effective.	systems, DoD captures all vaccine recipients and each anthrax vaccine immunization event in an automated database. This information is being used in database and potential cohort studies, and will facilitate any evaluation and treatment protocols that may be recommended in the future.
While an improved vaccine is being developed, use of the current anthrax vaccine for force protection against biological warfare should be considered experimental and undertaken only pursuant to FDA regulations governing investigational testing for a new indication. (Pg. 10 8, par. 1)	FDA has confirmed that AVA use against biological warfare is not an off-label use, nor is it subject to FDA's Investigational New Drug (IND) regulations.	Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of Anthrax Vaccine protects

		against inhalation anthrax. Therefore, I believe your interpretation is not inconsistent with the current label." Furthermore, a FDA 26 Nov 99 letter from Melinda K. Plaisler, Associate Commissioner for Legislation, in response to a letter from Congressman Dan Burton states, "Use of the vaccine for protection against both cutaneous and inhalation anthrax exposure is not inconsistent with the labeling for Anthrax Vaccine Absorbed." and "There is presently no basis for concluding that the anthrax vaccine, a licensed product, when used in accordance with current labeling, should be used pursuant to an IND application or, as requested in your letter, that FDA 'place the anthrax vaccine back under IND status'."
Under FDA regulations, use of an FDA-approved product in an unapproved way, or for an unapproved purpose, can only be undertaken pursuant to clinical trial protocols contained in Investigational New Drug (IND) applications. (Pg. 108, par. 2)	The anthrax vaccine is a FDA-licensed vaccine and is being used per the indications and usage on the package insert. The FDA in repeated testimony to Congress last year and in written communications continues to maintain that DoD's use of the anthrax vaccine for protection against inhalation anthrax is an appropriate use of the vaccine and is in accordance with the package insert.	"Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores. It is also recommended for high-risk persons such as veterinarians

		and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended. If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection." *Anthrax Vaccine Adsorbed Package Insert, BioPort Corporation, Lansing, Michigan U.S. License No. 1260.* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-

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Despite the fact the vaccine was approved as safe and subsequently deemed effective only against cutaneous anthrax infection, DoD asserts use of the FDA-approved AVA as prophylaxis against weaponized, inhalation anthrax does not constitute an off-label use against a new indication because while the package insert for this vaccine is nonspecific as to the route of exposure, DoD has long interpreted the scope of the license to include inhalation exposure, including that which	The package insert does not specify or limit the use of the vaccine for exposure to only the cutaneous form of anthrax. The FDA in repeated testimony to Congress last year and in written communications continues to maintain that DoD's use of the anthrax vaccine for protection against inhalation anthrax is an appropriate use of the vaccine and is in accordance with the package insert.	"Immunization with Anthrax Vaccine Adsorbed is recommended for individuals who may come in contact with animal products such as hides, hair, or bones which come from anthrax endemic areas and may be contaminated with *Bacillus anthracis* spores; and for individuals engaged in diagnostic or investigational activities which may bring them into contact with *B. anthracis* spores. It is also recommended for high-risk persons such as veterinarians

would occur in a biological warfare context. (Pg. 108, par. 4)		and others handling potentially infected animals. Since the risk of exposure to anthrax infection in the general population is slight, routine immunization is not recommended. If a person has not previously been immunized against anthrax, injection of this product following exposure to anthrax bacilli will not protect against infection." *Anthrax Vaccine Adsorbed Package Insert, BioPort Corporation, Lansing, Michigan U.S. License No. 1260.* Letter from Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration to Dr. Stephen C. Joseph, The Assistant Secretary of Defense of Health Affairs, March 13, 1997 reads: "While there is a paucity of data regarding the effectiveness of Anthrax Vaccine for prevention of inhalation anthrax, the current package insert does not preclude this use. The original efficacy trial clearly showed that the vaccine conferred a high level of protection against cutaneous exposure. None of the 5 inhalation cases in this trial occurred in Anthrax Vaccine recipients, but these data alone are insufficient to allow definitive statistical conclusions. Results from animal challenge studies have also indicated that pre-exposure administration of

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Since 1997, the *Department of Defense Nuclear/Biological/Chemical (NBC) Defense – Annual Report to Congress* has referred to medical CBW countermeasures proven safe because they have "been widely used to treat other medical conditions." The report cites pyridostigmine, bromide, the botulinum toxoid vaccine, both used for CB prophylaxis only pursuant to INDs, and the anthrax vaccine. (Pg. 109, par. 5)	Anthrax vaccine is not investigational. It is an FDA-approved vaccine and has been licensed since 1970.	Covered extensively above.
So the AVIP's cumbersome logistics, additional costs, and	The threat of weaponized anthrax to our troops is real	The new vaccine study, which is a tech-based effort to

increased risk of adverse reactions all flow directly from an unwillingness to do the research and testing to develop a better vaccine or improve the safety and efficacy of the current AVA. (Pg. 111, par. 4)	and is now. The AVIP's use of the current FDA-licensed anthrax vaccine is an appropriate, timely response to the current threat. Meanwhile, DoD continues to pursue a new, hopefully better vaccine through ongoing research, and continues an unprecedented program to monitor safety of the current vaccine.	develop a new vaccine candidate against anthrax, includes the following aspects: • Genetically engineering a new vaccine candidate based on Protective Antigen. The new vaccine candidate is called rPA. • Evaluating, selecting and optimizing an expression system. • Developing purification schemes. • Evaluating and selecting a vaccine adjuvant. • Demonstrating efficacy in animal models.
If DoD were to concede administration of AVA against inhalational battlefield exposure is an off label use, informed consent would be required. (Pg. 112, par. 3)	Anthrax vaccine is a licensed product and is not investigational.	Covered extensively above.
"A distinction must be made between treatment and experimentation. It may be asserted that anthrax vaccine (unlike pyridostigmine bromide as used in the Gulf War or anti-botulinum vaccine) constitutes 'treatment,' or that it is not experimental because of being declared safe and effective by FDA. ... In fact, the anthrax vaccine was licensed by the FDA before efficacy studies were required. Its efficacy against inhalational anthrax has been questioned.... British epidemiologist suggested that troops be publicly randomized to receive active vaccine or placebo, clearly implying that	The FDA in repeated testimony to Congress last year and in written communications continues to maintain that DoD's use of the anthrax vaccine for protection against inhalation anthrax is an appropriate use of the vaccine and is in accordance with the package insert.	In addition to the Department of Defense, other agencies and groups advocate or support the use of the anthrax vaccine. The Food and Drug Administration licensed the anthrax vaccine in 1970. The Centers for Disease Control & Prevention, the World Health Organization, the Armed Forces Epidemiological Board, and many other respected public health organizations support the use of the vaccine in persons at risk for exposure to *Bacillus anthracis*. Information about the AVIP and the anthrax vaccine is available on the Internet in a

many consider the vaccine to be experimental." (Pg. 113, par. 2)		variety of DoD web sites and in web sites such as the Center for Disease Control & Prevention and the Food and Drug Administration web sites. The web sites include facts about the vaccine, its history, side effects, purpose and more. Evidence for the efficacy of the anthrax vaccine is sufficient for it to be included in standard medical reference books in the United States and around the world. These references include: • *Control of Communicable Diseases Manual,* 16th ed. Abram S. Benenson, ed. "An official report of the American Public Health Association," Washington, DC, 1995. • *Guide for Adult Immunization*, Philadelphia: American College of Physicians, 1994 edition. • *Immunisation Against Infectious Disease*. Her Majesty's Stationery Office, London: British Joint Committee on Vaccination and Immunisation, 1996. • *Report of the Committee on Infectious Diseases*, 24th edition, Elk Grove Village, IL: American Academy of Pediatrics, 1997.

		• *ImmunoFacts: Vaccines & Immunologic Drugs.* Saint Louis: Facts and Comparisons, Inc., 1999. • *Merck Manual on Drugs & Therapeutics*. West Point, PA: Merck and Company, 1999. Anthrax vaccine is a prominent part of the World Health Organization's 1998 *Guidelines for the Surveillance and Control of Anthrax in Humans and Animals* (www.who.int/emc-documents/zoonoses/whoemczdi986c.html). Similarly, anthrax vaccination is specifically endorsed in the Working Group on Civilian Biodefense position paper on preparedness against anthrax (Inglesby et al. Anthrax as a biological weapon. *Journal of the American Medical Association)* 1999;281:1735-45; (www.ama-assn.org/sci-pubs/journals/archive/jama/vol_281/no_18/jst80027.htm). Officials at the CDC confirmed the validity of the vaccination guidelines in Inglesby's paper (MMWR 1999;48(Feb 5):69-74). ftp://ftp.cdc.gov/pub/Publications/mmwr/wk/mm4804.pdf The U.S. Department of Agriculture lists anthrax vaccine as a condition of employment for personnel of the Animal & Plant Health Inspection Service (APHIS),

		if potentially exposed on the job.
The AAPS recommended a careful examination of the medical ethics involved in military, and civilian, vaccination efforts, noting the entire point of informed consent in combat is 'not to prevent soldiers from obtaining whatever protection may be afforded them by an investigational agent that has not been adequately tested, but rather, it is to give them the choice of whether they think the 'protection' is worth the risks of adverse effect'" (Pg. 72, par. 1)	Anthrax vaccine is not an investigational new drug (IND).	Covered extensively above.
Although DoD's track record administering INDs or informed consent waivers is not exemplary, current procedural safeguards, adopted since the Gulf War, provide far more protection to service members receiving investigational products than the AVIP now provides. (Pg. 72, par. 3)	Anthrax vaccine is not an IND. This has no bearing and should be deleted from the report.	Covered extensively above.
In November 1997 the Subcommittee proposed, and the full Government Reform and Oversight Committee approved, an oversight report on Gulf War veterans' illnesses containing 18 findings and 18 recommendations. Among them was the finding that "the FDA was passive in granting and failing to enforce the conditions of a waiver to permit use of PB by DoD" and the recommendation that	This portion of the report has to do with PB as an IND and not with the anthrax vaccine. This portion of the report should be deleted since anthrax vaccine is not experimental, is not an IND, but is an FDA-licensed vaccine.	Covered extensively above.

"FDA should grant a waiver of informed consent requirements for the use of experimental or investigational drugs by DoD only upon receipt of a Presidential finding of efficacy and need." (Pg. 72, par. 4)		
Legislation reflecting that recommendation was introduced in both chambers of Congress. The 1999 Defense Authorization Act contained provisions, codified at 10 USC 1107(f), implementing the recommendation by strengthening notice requirements and by requiring a presidential authorization for any waiver of informed consent. (Pg. 73, par. 2)	This has to do with IND drugs and anthrax vaccine is not an IND.	Covered extensively above.
In view of the new statutory provision, FDA on October 5, 1999 revoked the 1990 interim final rule and issued a new regulation to govern DoD compliance with IND conditions and informed consent waivers. (Pg. 73, par. 3)	Anthrax vaccine is not an IND so this portion of the Subcommittee report does not apply.	Covered extensively above.
On September 30, 1999 the White House issued Executive Order 13139 establishing the procedures by which the president would comply with the new law. The EO says "[w]aivers of informed consent will be granted only when absolutely necessary " and only upon a written determination by the president that obtaining consent is not feasible, is contrary to the best interest of the service member	Anthrax vaccine is not an IND. This Executive Order 13139 is for granting permission to use an IND drug or vaccine; therefore, it does not apply to anthrax vaccine	Covered extensively above.

or is not in the interest of national security. In the event a waiver is granted, the DoD Secretary must notify Congress and publish a notice in the Federal Register. No waiver may last more than one year. Waivers may be renewed based on a new, fully documented request." (Pg. 73, par. 4)		